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Clinical laboratory tests

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In diagnosis and management of human disease, the most valuable assessment tools are usually the medical history and the physical examination. However, it is common for these to be supplemented with appropriate laboratory testing. Diagnostic tests may often lead to the ultimate diagnosis. The dentist should have knowledge of basic laboratory tests so that medically compromised patients can be skillfully handled. In addition, the dentist should feel confident in ordering certain tests, when warranted. Although diagnostic tests are valuable, they should only supplement medical history and physical examination, not replace them.

This paper will summarize some of the most commonly used clinical laboratory tests. It will focus primarily on blood tests, urinalysis and some cultures. Various biopsies will not be covered. It certainly does not include an exhaustive list of blood tests, as that would be beyond the scope of this paper. The attempt was to include those tests that are most commonly used to monitor patients with the most prevalent systemic diseases. 'Normal values' will be given in accompanying tables. These values were obtained from the Department of Laboratory Science at University Hospital in San Antonio. These values are guidelines and each practitioner should determine the 'normal values' for their particular laboratory.

It is important in this era of ever increasing medically compromised patient populations for the practicing dentist to establish a relationship with a clinical laboratory. These are available in hospitals and also as outpatient reference laboratories. It will take some effort on the dentist's part to seek out these resources, but this pre-emptive activity will save time later when laboratory values are needed. Some tests can be performed in the patient's primary physician's office. If the dentist expects to see large numbers of patients with a particular disease such as diabetes, it may be prudent to have a simple glucose monitor on hand in the office. However, when this information is obtained, the days of leaving this 'up to the physician' is no longer adequate. Laboratory testing will assume an even larger role in the routine management of dental patients in the future as our population ages with more chronic diseases.

Hematology

Hematology usually refers to an evaluation of the cellular components of the circulating blood. Hematologic tests may include the hemoglobin, hematocrit, red blood cell (RBC) count, RBC indices, white blood cell (WBC) count, differential count, platelet count, reticulocyte count and the sedimentation rate (Table 1). Certain tests such as the hemoglobin, the hematocrit, the RBC count, and the sedimentation rate will have significantly different values for men and women. Women will generally have lower values of RBC activity than men.

Hemoglobin

Hemoglobin is the essential oxygen carrier of the blood, and it gives the RBC its color. It allows oxygen to be absorbed and carbon dioxide to be released from the blood with normal respiration. It is reduced in hemorrhage and anemias and increased in hemoconcentration and polycythemia (1, 2). An adequate hemoglobin is particularly critical when patients undergo sedation or general anesthesia as respiration is often compromised. The normal values are presented in Table 1.

Hematocrit

The hematocrit is an instrument for measuring the relative amount of formed elements in plasma. However, the term is generally employed to indicate the volume of packed RBCs/100 mL of blood. Because of the

Table 1. Hematology values.

	Male	Female
Hemoglobin (gm/dL)	13.5–17.5	12.0–16.0
Hematocrit	41–53%	36–46%
Red blood cell count (million/mm^3)	4.5–5.9	3.8–5.2
MCV	80–98 FL	80–98 FL
MCH	26–34 pG	26–34 pG
MCHC	31–37 G/dL	31–37 G/dL
Reticulocyte count (percentage of red cell count)	0.5–2.5%	0.5–2.5%
Sedimentation rate	8 mm/h	15 mm/h
White blood cell count (thousand/μL)	3.6–11.0	
	Differential percentage of white cell count (thousand/μL)	
Neutrophils	40–80% 1.4–6.6	
Bands	0–5% 0–0.3	
Lymphocytes	20–50% 1.2–3.5	
Monocytes	2–12% 0–1.0	
Eosinophils	0–5% 0–0.5	
Basophils	0–1.2% 0–0.1	
Platelet count (thousand/μL)	150–450	

simplicity and high degree of reproducibility, hematocrits are easily carried out and are very accurate for predicting the degree of anemia. Changes in hematocrit will follow changes in hemoglobin as they both give a picture of RBC function (2). Normal values are presented in Table 1.

RBC count

RBCs are produced by the bone marrow and as mentioned above carry hemoglobin, the oxygen carrier of the blood. Anemia, or a decreased RBC count can be produced in two ways. The bone marrow does not produce enough RBCs as with the bone marrow cancer, leukemia, or the RBCs are destroyed too fast, as with hemolytic anemias such as sickle cell disease. If the bone marrow produces too many RBCs for the body to manage, then polycythemia is said to occur (1, 2). The normal values are in Table 1.

RBC indices

An estimation of the size and hemoglobin concentration can be determined by the use of RBC indices: mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC). These indices are helpful in targeting the etiology of various anemias. The MCH is the hemoglobin content of the erythrocyte and is determined by dividing the hemoglobin concentration times 10 by the RBC count. The MCHC is the concentration of the hemoglobin in erythrocytes and is determined by dividing the hemoglobin concentration times 100 by the hematocrit. The MCV is the average RBC volume and is determined by dividing the hematocrit times 10 by the RBC count. The RBC indices help to evaluate the RBC and its hemoglobin and will vary with their changes. For example, the MCV allows anemias to be classified according to RBC size. The patient has a microcytic anemia if the MCV is less than 80, a normocytic anemia if between 80 and 100, and a macrocytic anemia if greater than 100 (3). Also, patients with iron deficiency anemia will have a low MCHC (4). The normal values are presented in Table 1.

WBC count

The WBCs help defend the body against foreign microorganisms. Elevated WBC counts can be seen with acute infection and neoplasms. Other conditions that may raise the WBC count include exercise, emotional strain and anesthesia. A decreased WBC count may be seen in blood dyscrasias and in response to drug or chemical toxicity (5).

The differential count lists the percentage of the different types of WBCs. This is helpful because

changes in the percentage of cells may point towards a particular group of diseases. Neutrophils are increased in most bacterial infections. They are commonly decreased in certain blood dyscrasias and in response to cancer chemotherapy. The presence of immature WBCs is indicative of an increased production by the bone marrow. The most common of these cells is the banded neutrophil or band. These are often present with acute infection. The absolute neutrophil count (ANC) is determined by adding the neutrophils and banded neutrophils together. The ANC becomes very important in patients receiving cancer chemotherapy. ANC less than 500 significantly raises the potential for systemic life-threatening infection (6, 7). The eosinophils are increased in parasitic infections and allergic reactions. The basophils may be increased in blood dyscrasias. Lymphocytes may be increased with measles and chronic infections. Even though not listed with the differential, T lymphocyte counts are very important as predictors of potential for opportunistic infections in patients with HIV. This is particularly true with CD4 (T4) or helper lymphocytes. When the CD4 count drops below 200, the HIV patient is considered to have AIDS, as conditions associated with this syndrome are common (8). Monocytes may be increased during recovery from severe infections and Hodgkin's disease. The differential count is listed as the percentage of the total WBC made up by each particular cell. The normal values are presented in Table 1. The differential is listed as percentage of the WBC and also as absolute numbers.

Platelet count

The platelets are necessary for adequate hemostasis and to initiate the clotting of small vessels. Platelets can be increased in polycythemia and other diseases and are commonly decreased in diseases that involve the bone marrow. Decreased platelet counts are particularly common in patients receiving cancer chemotherapy (9). The normal platelet count is presented in Table 1.

Reticulocyte count

The reticulocytes are immature RBCs that are produced in increasing numbers in response to patients who have anemia. The bone marrow is trying to compensate for a lack of RBCs by increasing production. The reticulocyte count is expressed as a percentage of the circulating RBCs (1, 2, 10). The normal range is presented in Table 1.

Sedimentation rate

The erythrocyte sedimentation rate measures the settling speed for RBCs in fluid blood. At the end of 1 h, the number of millimeters, which the erythrocytes have settled is recorded. High sedimentation rates are seen in pregnancy, multiple myeloma, lymphoma, inflammatory processes and systemic response to tissue necrosis. Decreased sedimentation rate is seen in sickle cell disease (1, 2, 10). The normal values are presented in Table 1.

Urinalysis

Urinalysis is a commonly performed laboratory procedure that can provide valuable information (Table 2). It will help provide information relative to the functioning of the kidneys and the elimination of waste products of normal metabolism. Urinalysis is easily performed because it is a completely non-invasive test.

The volume of the urine should be approximately 1200–1500 mL/day. Polyuria is defined as a production of more than 55 mL/h of urine, and oliguria is defined as a production of less than 30 mL/h of urine. The clarity of the urine should be inspected for

Table 2. Urinalysis.

Volume	1200–1500 mL/day	
Clarity	Clear	
pH	5.0–8.0	
Color	Straw to amber	
Specific gravity	1.003–1.033	
	Males	Females
White blood cells (per high power field)	0–3	0–5
Red blood cells (per high power field)	0–3	0–3
Epithelial cells (per high power field)	<6	<6
Renal cells (per high power field)	<6	<6

clearness. Turbidity of the urine can be indicative of urinary tract infection. The reaction or pH of the urine is commonly evaluated. The normal pH of the urine is about 6 but can range from 5 to 8. The color of the urine may also relate to the clarity of the urine. Usually, the urine is yellow or reddish-yellow, according to the presence of several pigments. Brown or red urine can be indicative of bleeding somewhere along the urinary tract. The odor of the urine should have a characteristic aromatic odor. This can achieve an acetone smell in diabetics who are out of control.

The specific gravity of the urine is related to the kidney's ability to concentrate or dilute urine. The range of normal may be between 1.003 and 1.030. High fluid intake will result in a lower specific gravity of the urine, while a low fluid intake will result in a higher specific gravity of urine. The inability to concentrate or dilute the urine indicates kidney disease.

RBCs in the urine are indicative of bleeding somewhere along the urinary tract. WBCs in the urine are indicative of infection somewhere along the urinary tract. Bacteria in the urine commonly are seen with WBCs and are indicative of urinary tract infections. Protein in the urine is indicative of a number of kidney diseases (1). Casts in the urine are present because the albumin formed in the uriniferous tubules can be secreted. These may be indicative of kidney disease. They can also be helpful in determining where the disease process occurs in the kidney or if the disease is lower in the urinary tract (11). RBCs, WBCs, bacteria and casts are detected on microscopic examination of the urine. Glucose, ketones, bilirubin, protein and blood can be detected in the urine, using one of several test strips, which are dipped in urine and examined for color change (12).

Coagulation

Coagulation tests or tests of hemostasis are used to evaluate patients with potential bleeding disorders. Four commonly used screening tests include the prothrombin time (PT), the partial thromboplastin time (PTT), the platelet count and the bleeding time (BT) (Table 3).

Table 3. Coagulation values.

Prothrombin time	11–14 s
Partial thromboplastin time	23.5–34.3 s
Platelet count (thousand/mL)	150–450
Bleeding time	3–9 min

PT and international normalized ratio

The PT evaluates the extrinsic and common pathways of the coagulation phase of hemostasis. Most of the coagulation factors depressed by warfarin anticoagulation are in the extrinsic and common pathways, so patients taking these drugs will have an elevated PT. Close monitoring of these patients is critical, because there can be great variability in the degree of anticoagulation among patients on the same dose of medication (13).

In the past, the PT was used to monitor patients on warfarin anticoagulation. However, it was determined that since this test was not standardized among companies that produced it for clinical laboratories, there was much variation between PT results in the same patient depending on the laboratory used for the test. This variability has been corrected by the use of the international normalized ratio or INR. The INR is produced by compiling a PT ratio (PTR) of the patient's PT over the control PT for that laboratory and using an exponential multiplier called the international sensitivity index or ISI. The ISI is provided by the manufacturer of the test and corrects for the variability of testing reagents between companies. Therefore the $INR = PTR^{ISI}$. With the INR, the value will be the same no matter where the test is performed. The INR is now the standard for monitoring of patients receiving warfarin anticoagulation. The goal INR for these patients ranges from 2.0–3.0 for treatment of venous thrombosis to 2.5–3.5 for patients with mechanical heart valves (14–16). Table 4 shows INR values for a given PT with a given ISI.

Partial thromboplastin time

The PTT evaluates the intrinsic and the common pathways of the coagulation phase of hemostasis. Most congenital factor deficiencies, such as hemophilia, involve factors in the intrinsic pathway. Therefore, the PTT will be increased in these patients. Patients with severe liver disease will show elevated PTTs. Patients receiving heparin anticoagulation may be monitored with the PTT (13, 17). The normal PTT is given in Table 3.

Table 4. Relationship of the PT (s) to the INR.

PT	PT ratio	INR
10	0.84	0.8
11	0.92	0.9
12	1.01	1.0
13	1.09	1.1
14	1.18	1.2
15	1.26	1.3
16	1.34	1.4
17	1.43	1.5
18	1.51	1.6
19	1.60	1.7
20	1.68	1.9
21	1.76	2.0
22	1.85	2.1
23	1.93	2.2
24	2.02	2.3
25	2.10	2.4
26	2.18	2.5
27	2.27	2.7
28	2.35	2.8
29	2.44	2.9
30	2.52	3.0
31	2.61	3.1
32	2.69	3.2
33	2.77	3.4
34	2.86	3.5
35	2.94	3.6
36	3.03	3.7
37	3.11	3.9
38	3.19	4.0

Assume: GeoMean of controls = 11.9 s; ISI of reagent = 1.19.

Platelet count

The platelet count has been discussed earlier under the complete blood count. This test may be included both with the complete blood count and with coagulation tests. It is a test to evaluate the patient's platelet phase of hemostasis. Low platelet counts will commonly lead to elevated bleeding. The normal platelet count is listed in Table 3.

Bleeding time

The BT is used to evaluate both platelet quality and quantity. The test reflects the time between the making of a small incision and the moment when the bleeding stops. This will evaluate the hemostatic integrity of small vessels. Unfortunately, the BT test is not very sensitive and is not used much anymore. Recent dental studies have shown that the conventional BT test is not effective in predicting patients who will experience abnormal postoperative bleeding after dental procedures (18, 19). The normal range for this test is given in Table 3.

Chemistry

Chemistry commonly refers to tests of the blood that reflect ongoing metabolic processes. With current techniques, multiple tests can be easily conducted with as many as 20 tests performed at one time. Normal ranges for commonly ordered tests are presented in Table 5. These tests commonly should be evaluated as groups and not individually, because individual tests may be abnormal in the absence of disease. Also, normal variations of these tests may occur in certain common body processes, such as adolescent bone growth, pregnancy and aging. During the teenage years, active bone growth is occurring at a rapid rate. This is often reflected by significant increases in alkaline phosphatase. Because of bone composition, there may be slight elevations in calcium and inorganic phosphorus. Pregnant females may exhibit elevations of several tests, including glucose, cholesterol, total bilirubin and alkaline phosphatase. These are usually a reflection of increased stress placed on the female's metabolism by the fetus; however, alkaline phosphatase is produced by the placenta. These values should return to normal after delivery. In addition, physiologic aging

Table 5. Chemistry.

Alanine aminotransferase (ALT)		6–31 IU/L
Albumin		3.9–5.0 G/dL
Alkaline phosphatase		26–88 IU/L
Aspartate aminotransferase (AST)		11–36 IU/L
Total Bilirubin		0.2–1.2 mg/dL
Blood urea nitrogen (BUN)		5–22 mg/dL
Calcium		8.7–10.6 mg/dL
Carbon dioxide		18–30 mM/dL
Chloride		95–110 mM/L
Cholesterol		<200 mg/dL
Low-density lipoprotein (LDL)		<100 mg/dL
High-density lipoprotein (HDL)		≥ 60 mg/dL
Creatinine		0.5–1.5 mg/dL
Creatine kinase		24–196 IU/L
Creatine kinase MB		0.0–4.9 ng/mL
Gamma glutamyltransferase (GGT)		7–56 IU/L
Glucose		60–100 mg/dL
Lactate dehydrogenase (LDH)		110–222 IU/L
Magnesium		1.1–2.4 mg/dL
Inorganic phosphorus		2.7–4.5 mg/dL
Potassium		3.4–5.0 mM/L
Protein		6.2–8.1 g/dL
Sodium		135–148 mM/L
	Male	Female
Uric acid (mg/dL)	3.5–8.0	2.6–6.5

may show decreases in calcium, total protein and albumin (2).

Liver disease may result in abnormal values for several chemistry tests. These include total protein, albumin, cholesterol, total bilirubin, lactate dehydrogenase (LDH), alkaline phosphatase, gamma glutamyltransferase (GGT), aspartate aminotransferase (AST) and alanine aminotransferase (ALT). (Formerly, AST was referred to as serum glutamic-oxaloacetic transaminase (SGOT), and ALT was referred to as serum glutamic-pyruvic transaminase (SPGT).) (20) Primary liver disease shows an elevation in what are termed 'liver enzymes' (AST, ALT, GGT, LDH, alkaline phosphatase) and bilirubin. These five enzymes are present in the liver cell (hepatocyte). When these cells die due to pathology, the enzymes are lysed and picked up by the general blood circulation. Therefore, the serum value of these tests can be elevated in the presence of any pathologic process that destroys liver cells (21). Because AST is present in high levels in other organs, such as the heart, ALT is much more specific for the liver and is a more sensitive index of liver damage than AST. GGT is commonly used to evaluate the status of the liver in patients abusing alcohol as it becomes elevated with excessive intake (22). Bilirubin is formed through the breakdown of RBCs. Conjugation of bilirubin occurs in the liver; so in liver disease, the conjugation process is interrupted, resulting in increased total bilirubin (1). The above six tests can be elevated in many liver diseases, including hepatitis, alcoholic liver disease, obstruction and hepatoma (1, 20).

Calcium/phosphorus disorders may be evaluated with calcium, inorganic phosphorus and alkaline phosphatase chemistry tests. There is usually an inverse relationship between calcium and inorganic phosphorus. When calcium rises, inorganic phosphorus falls; when inorganic phosphorus rises, calcium falls. Diseases involving the mobilization of calcium from bone to serum will usually result in elevated calcium and alkaline phosphatase. Examples of this are metastatic carcinoma, multiple myeloma, osteoporosis, osteomalacia and Paget's disease (1).

Kidney disease is reflected by increases in blood urea nitrogen (BUN), creatine, uric acid and inorganic phosphorus. Elevation is due to compromised excretory function, resulting in increased serum levels. Decreased proteinemia may occur due to increased proteinuria, but this is not as specific as the above three tests. With increased inorganic phosphorus, the calcium level tends to decrease, and the body reacts by mobilizing calcium from bone, which is reflected by a rise in alkaline phosphatase. This body response is

termed 'secondary hyperparathyroidism' and is a common occurrence in chronic renal disease (1, 2).

The enzymes AST, LDH and creatine kinase (CK) are elevated in acute necrosis of the myocardium with *myocardial infarction*. Again, this is due to the lysis of myocardial cells, with resulting enzyme elevation in the serum. Isoenzymes of CK can help target the cell origin of lysis. CK-MB is specific for cardiac muscle. Diagnosis of myocardial infarction can be made with an increase in CK levels where CK-MB is at least 4–5% of the total (23–25). Elevation of cholesterol has been shown to be associated with an increased risk of coronary artery disease and myocardial infarction. Different types of cholesterol are associated with different risks of disease. Elevation of low-density lipoproteins (LDLs) is associated with an increased risk, and elevation of high-density lipoproteins (HDLs) is associated with a decreased risk of atherosclerotic disease (26–28). These tests have become very common in recent years as medication, particularly the statins, can control cholesterol levels and reduce the risk of myocardial infarction. C-reactive protein is a marker of inflammation. Atherosclerotic coronary artery disease has been shown to have an inflammatory component, and C-reactive protein elevation has emerged as a marker of cardiac risk (1).

Any process that will involve hemolysis of RBCs will result in an increase of LDH and total bilirubin. Rise in LDH occurs due to enzyme liberation after cell lysis, and rise in total bilirubin occurs because the body is not able to break down the increased number of hemolyzed RBCs. Hemolysis may occur due to hemolytic anemia, drug reactions and other systemic causes.

Elevated uric acid is an indicator of rapid protein synthesis, which is seen in malignant diseases, such as *lymphomas* and *leukemias* (1, 2). LDH increase may also occur in malignant neoplasms due to rapid cell turnover. Increased total protein is seen in the dysproteinemias, such as *multiple myeloma*. Since this is an increase of the globulin fraction of protein, the albumin is usually normal (1, 2).

Serum glucose is increased in patients with *diabetes mellitus*. Glucose levels vary greatly depending on food ingested and time of day. Diagnosis of diabetes mellitus is made if the patient has any symptoms of diabetes and a random glucose of $\geq$200 mg/dL or a fasting glucose of $>$125 mg/dL after an 8-h fast or a glucose $\geq$200 mg/dL 2 h after beginning an oral glucose tolerance test (29). Even though not a chemistry test as such, hemoglobin A1c or HbA1c is a long-term marker of glucose regulation and is used to monitor diabetic control. Definitive reference ranges still have to be established, but in general HbA1c $<$7% is associated with good control and $>$10% is associated with poor control (30). HbA1c of $<$7% lowers the risk for the development and progression of microvascular disease associated with diabetes mellitus (1). One of the most common sequelae of diabetes mellitus is involvement of the vasculature of the kidney. This may result in compromised kidney function with elevation of the appropriate tests.

Serum electrolytes (sodium, chloride, potassium and carbon dioxide) are often measured together or as part of a multitest screen. These tests are used to monitor fluid and electrolyte balance. Out of control diabetics in ketoacidosis have major changes in their fluid and electrolyte balance. This is often the acute life-threatening emergency in these patients. Close monitoring and management of serum electrolytes is necessary to stabilize these patients prior to addressing glucose control (1, 2).

Immunology and virology

In the past, an important area of laboratory medicine was serology. Serology refers to the testing of blood for antibodies that are specific for certain diseases. Originally, most of the available tests were for syphilis. However, with the virtual explosion of infectious disease antibody testing and looking for antibodies in a large number of autoimmune diseases, this area has expanded beyond simple serology. The science of virology has grown greatly in recent years. Serology played an important role here, as most diseases were diagnosed by looking for antibodies in certain viruses as culture and other testing were not available. Virology has expanded beyond serology to include culture and molecular diagnosis. For the above reasons, it seems reasonable to collate this group of tests under immunology and virology.

Various serologic tests are available to evaluate blood for past presence of infection with *syphilis*. The Venereal Disease Research Laboratory (VDRL) and the rapid plasma reagin (RPR) tests detect flocculation or particle clumping that is initiated by non-specific antibodies in the serum of patients with syphilis. The fluorescent treponemal antibody-absorption test of syphilis (FTA-ABS) is the reference test for syphilis and determines

the binding of the patient's antibodies by direct immunofluorescence to *Treponema pallidum*. This test is conducted to confirm whether positives from the screening tests, such as the VDRL and the RPR, are in fact true positives (31, 32).

Infectious mononucleosis is caused by the Epstein–Barr virus that infects B lymphocytes. Serologic detection of this infection employs a heterophile antibody test that identifies antibodies to this virus in the patient's serum (1).

Serologic tests are available to evaluate patients with viral hepatitis (see Table 6). These are very valuable in making the diagnosis and following the progression of the disease. *Hepatitis A* is screened by the detection of hepatitis A antibody or anti-HAV. The IgM fraction will be elevated for acute disease and for 3–6 months after infection. Following infection or vaccination, the IgG fraction will be present, indicating protection against re-infection (33, 34).

Hepatitis B produces several markers that are helpful in the diagnosis of the disease. The hepatitis B surface antigen (HbsAg) will be present in patients who have acute infection with hepatitis B. A certain percentage of patients who are exposed to hepatitis B will become chronic carriers for the HBsAG. This test can be conducted to evaluate whether patients become chronic carriers. After the infection and the patient develops immunity, patients will develop hepatitis B surface antibody (anti-HBs). Detection of this antibody means that patients have an immunity against hepatitis B infection and it is present when patients have responded to vaccination. There is a 'window period' between the time that the HBsAg falls and the anti-HBs rises that neither test will be positive. This 'window period' can be evaluated using the hepatitis B core antibody (anti-HBc). Therefore, to evaluate a patient for acute infection with hepatitis B, one should employ the HBsAg, the anti-HBc and the anti-HBs. Hepatitis B e antigen or HBeAg is indicative of a high degree of infectivity with the virus (33, 34).

Table 6. Screening tests for viral hepatitis.

Type	Test	Significance
Hepatitis A	Anti-HAV	IgM with acute infection IgG with immunity
Hepatitis B	HBs Ag	Acute infection, carrier state
	Anti-HBs	Immunity
	Anti-HBc	Positive between HBs Ag and Anti-HBs
	HBe Ag	Patient is highly infectious
Hepatitis C	Anti-HCV	Indicates infection but does not necessarily confer immunity
Hepatitis D	Anti-HDV	Indicates infection
Hepatitis E	Anti-HEV	Indicates infection

Hepatitis C antibody or anti-HCV is used as a screening test for *Hepatitis C*. However, it may not become positive for 12–16 weeks after exposure. HCV RNA testing can be positive as early as 4 weeks after infection and can be used to follow progression of therapy. This may be important because chronic progression of disease is very common. There is no carrier state for hepatitis C (35).

Hepatitis D and *E* can both be evaluated by detecting antibodies formed after infection. These are anti-HDV and anti-HEV, respectively (33, 34).

Another commonly used serologic test is for the diagnosis of *human immunodeficiency virus* (*HIV*) infection. This test will detect circulating antibodies against the virus. Positive tests are confirmed with the Western blot confirmatory test (8). As mentioned earlier under the Hematology Section, CD4 lymphocyte count is important in the monitoring of HIV patients as counts of less than 200 greatly increase the risk for opportunistic infections. Viral load is also used as an indicator of progression of disease and of response to treatment. Greater than 5000 copies/mL is suggestive of disease progression and less than 5000 copies/mL is the target for successful treatment (36, 37).

Patients with *autoimmune disorders* produce antibodies to their own tissues, which initiate the inflammatory destruction associated with these diseases. The antinuclear antibody test or ANA will be positive in many of these patients, including those with systemic lupus erythematosus, scleroderma, Sjögren's syndrome, polymyositis and rheumatoid arthritis. The ANA tends to be a sensitive test in these individuals, but not very specific. Therefore not all of these patients will have a positive test. More specific tests can be conducted to target individual diseases. For example with Sjögren's syndrome, a disease that commonly results in xerostomia, only 75% of patients will be ANA

positive. The ANA can be followed up with antibody tests to SS-A and SS-B, where over 90% of Sjögren's syndrome patients will be positive (1). This information along with clinical signs and symptoms ultimately lead to diagnosis (38, 39).

Microbiology

Patients who exhibit oral infections should have bacteriologic culturing performed, if possible. Unfortunately, due to the rich supply of bacteria in the oral cavity, this culturing is commonly misleading at best and completely worthless at worst. It is important to try to obtain anaerobic aspirates of infections so that cultures can be grown both on aerobic and anaerobic media. If cultures are positive, susceptibility testing can be conducted to determine the use of appropriate antibiotics. In reality, most patients respond well to first-line antibiotics for oral infection. However, in the small percentage of patients who do not respond to these drugs, susceptibility testing can be very important.

Patients who exhibit signs of *Candida* infections in the mouth need appropriate diagnostic testing to confirm the diagnosis. Culture of these areas can be performed, but this can be misleading, since up to 60% of the normal population will be carriers of *Candida* in their mouth and will grow organisms on culture. Culture may be critical, however, in confirming the diagnosis of erythematous candidiasis, as this form does not lend itself to the cytological methods listed below. Tests that can be conducted much more quickly and lead to a rapid diagnosis of pseudomembranous candidiasis include the Gram stain, potassium hydroxide (KOH) wet preparation or exfoliative cytology. The Gram stain is rapidly performed on a specimen placed on a glass slide. Pseudohyphae and *Candida* conidia can be appreciated as they stain intensely Gram-positive. The KOH wet prep is conducted by dropping 10% KOH on the specimen placed on a glass slide and looking for the same pseudohyphae and conidia (2).

It is extremely important in patients who are immunocompromised to be able to employ diagnostic testing to confirm *herpes simplex virus* (*HSV*) infection. These infections cannot be diagnosed on clinical grounds alone and must be confirmed by diagnostic testing. Culture remains the gold standard to diagnose this infection and is obtained by swabbing the suspicious lesion. The laboratory then plates this material on cell lines that are specific for viral damage. A positive test is reported if a specific cytopathic effect is seen on the cells. Culture commonly takes a minimum of 48 h to be reported as positive. Other tests are available that are quicker, but have less sensitivity than culture. These include direct immunoperoxidase, ELISA and exfoliative cytology (2, 40). It is important for the health professional to determine and understand the HSV testing available to him or her, because not all tests will be available in each area.

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